

# The Madras Clinical Journal

Vol. XXIX

July 1962.

No. 1

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# The Madras Clinical Journal

JOURNAL OF THE MADRAS STATE BRANCH OF THE INDIAN MEDICAL ASSOCIATION  
(WITH WHICH IS INCORPORATED THE "MISCELLANY")

Vol. XXIX

July 1962

No. 1

## MEDICAL ASPECTS OF DISEASES OF THE PANCREAS \*

Dr. G. VICTOR, M. D.,  
Professor of Medicine, Madura Medical College.

### PHYSIOLOGICAL CONSIDERATIONS :

The pancreas is both an *exocrine* and an *endocrine* gland. Its external secretion by virtue of its *enzymic* content plays an important role in the digestion of all the major food stuffs, viz., proteins, fats, and carbohydrates. It also supplies large quantities of bicarbonate which help to neutralise acid gastric chyme and to provide an alkaline medium in the small intestine favourable to the activities of its own ferments. *Insulin* is the internal secretion of the pancreas and it regulates the carbohydrate metabolism. In the fasting state, only small amounts of pancreatic juice are secreted, but during digestion there is a copious flow, which is stimulated by both nervous and hormonal influences. The presence of acid in the duodenum evokes the secretion of a considerable volume of pancreatic juice high in bicarbonate but low in enzymes. This secretion can be attributed to stimulation of

the pancreas by "secretin" hormone which is liberated from the mucous membrane of the small intestine. When "pancreozymin" extract from the mucosa of the small intestine is given intravenously, it stimulates the secretion of pancreatic juice rich in enzymes.

The protein-splitting enzyme of pancreatic juice "*trypsin*" is probably a combination of 2 or 3 enzymes. The trypsin group of enzymes reduces proteins to proteoses and peptides. Pancreatic *lipase* splits fats to glycerine and fatty acids. Pancreatic *amylase* reduces starch and glycogen to maltose.

If the external pancreatic secretion is insufficient, stools are characteristically bulky, light-coloured, greasy and contain excess quantities of total solids, fat and nitrogen. The passage of free oil or of butter-like masses on the surface of the stool is pathognomonic of pancreatic insufficiency.

\* Lecture delivered at the 34th Annual Conference of the Madura Medical Association.

The presence of large numbers of striated muscle fibres from dietary meat in the faeces and of excess quantities of nitrogen is characteristic of this condition (and may also occur in small intestine insufficiency).

**Pancreatic Juice:** The pancreas secretes a colourless, odourless, alkaline fluid of low viscosity, tasting strongly of sodium bicarbonate. The distinguishing chemical characteristic of the juice is its high *bicarbonate* content. The bicarbonate and *chloride* concentration of pancreatic juice vary in a reciprocal manner so that the sum of the two expressed in milli-equivalents is approximately constant and nearly the same as the total base of the blood plasma. In addition to chloride and bicarbonate, the pancreatic juice contains a small amount of phosphate, but less than that occurring in blood plasma. The principle bases of pancreatic juice are *sodium*, *potassium* and *calcium*. The concentrations of sodium and potassium are approximately equivalent to those of the blood plasma. Since much of the blood calcium is combined with proteins and is not in a diffusible state, its concentration is only 3–4 mgm% as compared to about 10 mgm% for blood. The *protein* content of pancreatic juice varies over a wide range, but in an orderly manner with the conditions governing secretion. Concentrations found in human pancreatic juice are nearer the lower extreme ranging from 0.1 to 0.3%. *The protein in the juice consists mainly of enzymes.* *Proteolytic* activity is found in one component, *lipolytic* activity in another, and *amylolytic* activity yet in another. The relative concentrations of the different enzymes in the juice can be made to vary by using different stimuli to cause secretion.

The proteolytic enzymes as they occur in the pancreatic tissue and freshly secreted pancreatic juice possess no proteolytic activity and are referred to in that state as “zymogens”. In older literature the proteolytic activity was attributed to trypsin, the corresponding zymogen being trypsinogen. Spontaneous activation of trypsinogen is suppressed by crude extracts and also in the living pancreas, by the process of an inhibitor which inactivates small amounts of trypsin. Kunitz and Northrup have shown that trypsin or trypsinogen consists of two components viz., *trypsin* and *chymotrypsin*. The *peptides* resulting from protein digestion by trypsin and chymotrypsin are further digested by enzymes called “*peptidases*”—most of these come from the intestinal mucosa. One has been isolated from pancreatic juice called *carboxypeptidase* which splits off the end-amino acid containing a free carboxyl group from polypeptidase. In fresh pancreas it occurs in an inactive form “*procarboxypeptidase*” and is activated by trypsin.

The ability of pancreatic juice to emulsify and hydrolyse fats is due to a single enzyme called “*pancreatic lipase*”. This hydrolyses fat only in the presence of bile-salts or other substances with similar properties. The bile salts in higher concentration inhibits the action of lipase. The pH at which the pancreatic lipase exhibits its optimum activity varies with the substrate, but is always on the alkaline side of neutrality.

The amylolytic activity of pancreatic juice is due to *pancreatic amylase*, which may be one or two enzymes. Pancreatic amylase is secreted in an active form and chloride is the most efficient activating ion. The optimum

pH for activity of pancreatic amylase varies between 6·5 and 7·2 depending upon the kind and concentration of neutral salts present in the solution.

Pancreatic juice also contains ribonuclease and desoxyribonuclease which partially hydrolyse the corresponding nucleic acid into mononucleotides. The optimum pH for desoxyribonuclease is in the neighbourhood of 7.

The pancreatic enzymes are important for digestion. If the pancreatic juice is excluded from the intestines (by pancreatectomy or ligation of ducts), impairment of digestion and absorption of various food stuffs would result. This is most pronounced in the case of fat and protein and unabsorbed fat appears in large

amounts in the stools, called "steatorrhoea". The bicarbonate of the juice seems to neutralise the gastric juice as it enters the intestine and produces a pH more favourable for intestinal digestion.

Bayliss and Starling discovered *secretin* in 1902. It is a polypeptide with a molecular weight of 5,000. Stein and Ivy have shown that secretin is destroyed by an enzyme found in the blood and urine which they called "*secretinase*". In 1943 Harper and Raper produced a factor which did not increase the volume of pancreatic juice, but did greatly increase the enzyme concentration. This substance they called "*pancreozymin*". Hydrochloric acid in the intestine liberates "*secretin*" into the blood thus causing the pancreas to secrete.

## PANCREATIC PHYSIOLOGY

### ENZYMES :

Inactive  
Proteolytic  
Enzymes called  
"Zymogens"

### PANCREAS

#### EXOCRINE

#### ENDOCRINE

Insulin

- |   |   |                                     |   |
|---|---|-------------------------------------|---|
| <ol style="list-style-type: none"> <li>1. Trypsin<br/>(Trypsinogen + Enterokinase)</li> <li>2. Chymotrypsin</li> <li>3. Carboxypeptidase</li> </ol> | } | + Proteins =                        | Polypeptides (Proteoses, Peptides) and Aminoacids (Leucine, Tyrosine) |
| <ol style="list-style-type: none"> <li>4. Lipase + Neutral Fats — (Triglycerides)</li> </ol>  | } | [ in the presence of bile - salts ] | = Diglycerides, Monoglycerides, Free fatty acids, Glycerol.           |
| <ol style="list-style-type: none"> <li>5. Amylase + Starch and Glycogen</li> </ol>  | } | [ in the presence of chloride ]     | = Maltose.  |
| <ol style="list-style-type: none"> <li>6. Ribonuclease, Desoxyribonuclease</li> </ol>   | } | + Nucleic Acid =                    | Mononucleotides.  |



**MINERAL SALTS :**

Sodium bicarbonate — (0.3 — 0.65%) — Neutralises gastric juice.  
 Sodium chloride — 8 Grams  
 Phosphate,  
 Sodium, Potassium, Calcium.

**INFLUENCED BY :**

- (a) **SECRETIN** — Polypeptide from small intestinal mucosa, liberated by Hcl. *Increases* volume of duodenal fluid, bicarbonate concentration (6 or 7 times), alkali concentration (40 times), *fall* of concentration of all pancreatic enzymes.
- (b) **PANCREOZYMIN** — Produces flow of juice rich in enzymes, degeneration of pancreatic cells, increases enzyme concentration.

**DISEASES OF THE PANCREAS :**

The following are the diseases of the pancreas which are of interest to the physician :

1. Acute Pancreatitis
2. Chronic Pancreatitis
3. Islet-cell Tumour of the Pancreas
4. Carcinoma of the Pancreas

**CLINICAL FEATURES AND DIAGNOSIS :**

(a) *Acute Pancreatitis* : The clinical picture varies with the intensity of the pathological process. *Pain* is either sudden or gradual in onset, but is severe and persistent (excruciating), it may continue for many days. It is located in the epigastrium or either upper quadrant of the abdomen, and is referred to the dorso-lumbar region of the back, lower abdomen, or shoulders. Long continued severe pains in left upper abdominal quadrant and back is characteristic of pancreatitis. *Shock* occurs only in patients having severe necrosis or haemorrhage. Vomiting is obstinate. *Obstination, distension, ileus* are common, but diarrhoea is unusual. *Fever* is usually present. *Chills and transient jaundice* may sometimes occur.

Physical signs are meagre. *Tenderness* in the epigastrium or upper abdominal quadrants with abdominal distention is a common finding. A tender epigastric mass can be palpated in a few patients a week after the onset of symptoms. A bluish *ecchymotic* discolouration of the skin of the flanks (Turner's sign) or about the umbilicus (Cullen's sign) occurs with severe haemorrhagic necrosis.

**Diagnosis :** 1. A marked and protracted elevation in serum enzyme activity is observed only in patients with acute haemorrhagic pancreatitis. 2. Extremely elevated values for a serum amylase usually signifies a diagnosis of acute primary pancreatitis (Abruzzo *et al*). 3. Concentration of serum amylase becomes elevated within a few hours after the onset of the attack and usually returns to normal in 36 - 72 hours. The concentration of lipase in the serum increases more slowly and remains elevated for longer periods. 4. In patients with oedematous pancreatitis, temporary increase to the upper limit of normal were noted. 5. In all cases of acute oedematous pancreatitis, an elevation was present ranging from 1400 to 1800 units. 6.

An increased amount of antipyretic activity in the plasma of patients with acute pancreatitis was demonstrated by Goldstein *et al.* 7. An excess secretion of lysine in the hereditary group of persons with pancreatitis was noted by Gross. 8. Foulk and Fleisher found the glutamic oxalacetic transaminase activity increased in patients with acute pancreatitis. 9. In Ruternberg's series, serum leucine aminopeptidase activity was increased in 4 of the 6 patients with acute pancreatitis. 10. Saxon and Budd have reported the value of urine diastase in the diagnosis of pancreatic disease. Often it is a more sensitive index of continuing pancreatitis than the serum enzyme determination. 11. Transient hyperglycaemia with glycosuria and also transient hyperbilirubinaemia are found in some cases of acute pancreatitis. 12. Reduction in serum calcium may occur. 13. Albuminuria, cylindruria, and microscopic haematuria and leucocytosis are common laboratory findings.

**Differential Diagnosis:** Ruptured peptic ulcer, intestinal obstruction, diseases of biliary tract.

(b) *Chronic Pancreatitis:* Functionally, external pancreatic insufficiency and diabetes mellitus are the end results. The clinical syndrome of chronic pancreatitis is divided into two stages: (i) An early stage characterised by repeated attacks of acute pancreatitis without evidence of permanent damage to the gland. (ii) A late stage, when a permanent functional impairment of the pancreas occurs and calcification of the gland is found radiologically.

Painful episodes are present for longer periods. This alternates with periods of no symptoms.

(c) *Islet-cell Tumours:* The symptoms are those of *hypoglycaemia* due to an excess of endogenous insulin. Fatigue, hunger, perspiration, apprehension, many mental and nervous phenomena are constant. The clinical picture includes apathy, irritability, restlessness, confusion, excitement, disorientation, delusion, convulsions, mania, stupor, coma, etc. These symptoms come on long after meals and after exercise.

Patients with hyperinsulinism often learn to ingest large amounts of carbohydrates for temporary relief of symptoms and thus they tend to become obese. Attacks of *nervous or mental disturbances* that occur during the fasting states, are associated with concentrations of blood sugar of 60 mgm% or lower and are promptly relieved by the administration of glucose.

The pathological changes of the exocrine pancreas or of adjacent organs may be an abnormal stimulation of the vegetative nerve fibres in the pancreatic or parapancreatic region give rise to hyperinsulinism or hyperplasia and adenomata of the islands of Langerhans or both.

(d) *Carcinoma:* Pain is the cardinal symptom in 3 of every 4 cases of carcinoma of pancreas. Only in one of four, painless *jaundice* occurs. It is constant and boring in type, is located in the upper part of the abdomen and extends to the back. Gradually it gets more severe. *Loss of weight, weakness, fatigue, anorexia, nausea, vomiting and constipation, delirium, mental depression and anxiety* occur. Jaundice appears sometime during the course of the development of carcinoma involving the head of the pancreas, then there is severe *pruritus*.

Physical signs include loss of weight, jaundice, mass in upper abdomen, enlarged, liver and distended gall-bladder. Ascites will be present only in advanced cases with metastases. Slight degree of anaemia is common.

Abdominal pain or distress is the most frequent initial symptom. In Bell's series, 9 patients presented with *thrombophlebitis*, there was high incidence of *glycosuria* and *hyperglycaemia*. Carcinoma probably produces glycosuria more by interference with the escape of insulin from the pancreas than by actual destruction of the islets. Clifton mentions *emotional disturbance* especially depression and anxiety as early manifestations. *Diarrhoea* developing in elderly patients without demonstrable cause should always suggest pancreatic carcinoma. If there is partial obstruction to the pancreatic duct, duodenal intubation may show deficient bicarbonate and sometimes frank blood-staining of the duodenal juice.

Ruternberg and associates have reported that the serum leucine aminopeptidase level is also raised in patients with carcinoma of the pancreas.

Normal leucine aminopeptidase rules out cancer of the head of the pancreas.

High serum levels in patients with cancer imply a poor prognosis.

#### INVESTIGATION OF PANCREATIC DYS-FUNCTION:

**Introduction:** Pancreatic lesions often escape detection. In less than half the cases of acute pancreatitis, a correct diagnosis is established. In cancer of the pancreas the early symptoms are rarely recognised, until the

spreading disease involves some contiguous structure such as the common bile-duct.

**Clinical Approach:** "No symptoms are pathognomonic of pancreatic disease". We rely on tests of pancreatic function to confirm a clinical suspicion that the pancreas is involved. Changes in both external and internal secretion of the pancreas may accompany pancreatic disease; in most instances pancreatic function is depressed.

Pancreatic dysfunction may be revealed by the following abnormalities:—

1. Increased concentration of the pancreatic enzymes in body fluids.
2. Diminished secretory capacity of the pancreas.
3. Abnormal carbohydrate tolerance.

**I. Examination of Serum, Urine and Peritoneal fluid:** (Amylase, lipase, alkaline phosphates and antithrombin). In *acute cases*, blood is taken (a) on admission and (b) every 12–24 hours during the very acute stage. The optimum time for elevation of *serum amylase* is a period beginning 6 hours after the onset of the attack and ending by the 4th day. For *serum lipase*, beginning either a few hours or 24 hours after onset and ending between the 4th and 11th day. In *chronic cases*, blood is taken (a) fasting, (b) at the height of digestion (3 hours after a meal), (c) several times especially during periods of exacerbation, and (d) after injection of secretin or prostigmine. It is essential to determine amylase and lipase. Properly repeated examinations will detect transient hyperenzymemia (i. e. elevated serum amylase and/or lipase).

**Serum Antithrombin Test.** It is done for acute pancreopathy. Positive results are supposed to be most frequent, persistent, and specific than elevation of serum amylase and lipase. This test is based on the rise of antithrombin in experimental hypertrypsinemia. It is an indirect test of elevated serum trypsin. The test was positive in 91% of 55 cases of acute pancreopathy, beginning 3 hours after the onset of symptoms and lasting throughout the acute phase. The increase amounted to 600% of the normal values. Maintenance or rise of elevated antithrombin level suggests persistence or extension of the damage, eg. transition from the oedematous-interstitial to the necrotic-haemorrhagic type.

**II. Direct Estimation of Pancreatic Secretory Capacity.** Examination of duodenal contents: Pancreatic function can be estimated directly by duodenal intubation. This method is not entirely satisfactory, for duodenal contents are an admixture of fluid derived from the intestine, biliary tract and pancreas.

(a) **Secretin Test:** One clinical unit of secretin per Kgm. body weight is given, test is continued for 80 minutes, and the normal values obtained are as follows:— (1) Total volume = 2 ccs/Kgm., (2) Maximum bicarbonate concentration = 90 mil. eq/litre, (3) Amylase out-put = 6 Units/Kgm. In pancreatic disease, there may be 2 main types of abnormal response: *Type I* — Present during the first 2 weeks of the recovery phase after mild or moderately severe acute pancreatitis. The enzyme secretion is depressed, there is a reduction in the output of amylase, values for trypsin and lipase may be less affected. *Type II* — Found when irreversible changes have taken place

in the pancreas due to necrosis, fibrosis or duct obstruction. Fall in both enzyme and bicarbonate out-put occurs.

(b) **Fasting Test:** Indicates the response to the physiological, intrinsic, interdigestive stimulation. It stimulates water, bicarbonate, and enzymes. (a) Volume — ranges from 0-30 cc per 20 minutes. (b) Concentration of the enzymes — hyperconcentration indicates irritation of the pancreas. Marked hyposecretion suggests deficiency. (c) Bicarbonate secretion is very low and does not give any information concerning the ability of the pancreas to secrete it.

(c) **Vagus Test:** This assays the output of enzymes. A normal result rules out severe deficiency of the respective enzyme secretion. A subnormal result is evidence of severe deficiency. Supranormal volume and/or of enzyme concentration indicate an irritation of the pancreas. Following a "fasting" or "secretin" test, 15 units of insulin or 0.2 units/kgm. are given intravenously or 15 mgm. urecholin subcutaneously. The duodenal content is collected in fractions of 10 or 20 minutes for a period of 40 or 60 minutes.

(d) **Oil Test:** 20 ccs. of olive oil free from fatty acids is warmed to body temperature and introduced into the duodenum. Collect duodenal contents in 10 or 20 minutes fractions. Normal result rules out deficiency of enzyme secretion. Subnormal concentration of enzymes represents severe or moderate deficiency. Supranormal enzyme concentrations and/or volumes indicate hypersecretion by an irritation of the pancreas.

(e) **Triple Test:** This is a combined fasting-secretin-vagus Test. Comparative administration of the

secretin-vagus tests with the fasting-oil tests is carried out. The secretin-vagus tests cover the water-bicarbonate and the enzyme secretion and measure the secretory capability of the pancreas itself. The fasting-oil tests also include the extra-pancreatic control. Comparison of the results of both groups permits differentiation between deficiency of the pancreas from deficiency of the extra-pancreatic control.

### III. Evidence of impaired digestion and absorption of food :

#### (a) Examination of stools :

(i) Inspection of the stools—In gross deficiency of external pancreatic secretion, the stools are bulky and fat. If in addition blood is present, the stools may appear to have been smeared with silver or aluminium paint.

(ii) Microscopically—Stools from a patient on a mixed diet will show highly refractile neutral fat globules and undigested meat fibres.

#### (b) Enteral assimilation tests :

Existence of impaired assimilation is shown by increased fat, increased undigested muscle fibres, undigested nitrogen, and undigested starch. Pancreatic origin of impaired enteral assimilation is concluded from :

- (i) Deficiency in duodenal pancreatic function tests.
- (ii) Excessive degree of steatorrhea.
- (iii) Marked degree of creatorrhea, or of azotorrhea.

(c) *Trypsin test in the faeces* : In infants, complete absence indicates absence of external secretion which means severe obstruction and/or destruction of the pancreas.

### IV Examination of Blood glucose and Urinary glucose :

(a) *The Triolein Absorption Test* : Balash & Williams studied 20 patients with hyperglycaemia. All had elevated fasting and 2-hour post-prandial blood sugar levels or diabetic type glucose tolerance curves. After blocking the uptake of  $I^{131}$  by the thyroid gland with Lugol's solution, 25 - 50 microcuries of  $I^{131}$  labelled Triolein or Oleic Acid in capsule form were administered with 240 cc. of milk to fasting patients. Venous blood, urine, and stools specimens were assayed for radioactivity by conservative methods and the results expressed as percentage of the ingested dose. Normal range—(a) Percent ingested dose ( $I^{131}$  labelled Triolein) in 0-48 hours urine is 44 - 91%. (b) Percent ingested dose ( $I^{131}$  labelled Triolein) in 0-48 hours stool is 0.2-9.0%. This test offers a direct measurement of pancreatic exocrine function.

(b) *The Starch Tolerance Test* : Used by Avery Jones in pancreatic insufficiency, is based on a comparison of the blood sugar response to a glucose tolerance test with that obtained after starch. The interpretation of the test is based on the assumption that pancreatic amylase is the major physiological substance responsible for hydrolysing starch in significant amounts under the conditions of the test. If the starch tolerance test is positive, it has thus far proved to be a reliable indicator of pancreatic disease. On the other hand, a negative starch tolerance test does not rule out pancreatic disease.

V *Laparotomy and Biopsy* : White spots of necrosis on the serosa may be found. Biopsy from suspected areas from more than one site may

be essential. Intra-operative needle biopsy of the pancreas may yield more information.

# REFERENCES

- Balash, W. R., Williams, C. M.: "Latent Pancreatic exocrine insufficiency in patients with Hyperglycaemia". *Amer. Jl. Med. Sciences*, 242, 2, Aug. 1961, pp. 193.
- Best, C. H., Taylor, N. B.: "Pancreas, Liver, and Biliary Systems". *The Physiological basis of Medical Practice*. 7th Edn, 1961.
- Bressler, B. R., Forsyth, G., Klatskin: *Jl. Lab. & Clin. Med.* 56, 3, Sept. 1960, pp. 417.
- Cecil, R. L., Loeb, R. F.: "A Text book of Medicine". 10th Edn, 1960 (Rep).
- Flogh, M. H., Groisser, V. W.: "Serum Proteolytic enzyme activity in Pancreatic Disease". *New Eng. Jl. Med.* 263, 22, Dec. 1960, pp. 1129.
- Friedlander, E. O.: "Hyper-Insulinisms in Pancreatic Biliary and Gastro-intestinal Tract Disease". *J. A. M. A.* Aug. 5, 1961, pp. 300.
- Henke, W. J., Vacca, J. B., Van Goidsenhoven, G. E., Knight, W. A. "Evaluation of Pancreatic Functional tests in confirmed Pancreatic Disease". *Gastro-enterology*, 41, 3, Sept. 1961, 233.
- Howat, H. T.: "Investigation of Pancreatic dysfunction". *Modern Trends in Gastro-enterology*, 1958.
- Johnson, T. A., Kalser, M. H.: "The Pancreas". *Gastro-enterology*. 39, 4, pp. 469.
- Pimparker, B. D., Tulsky, E. G., Kalser, M. H., Bockus, H. L.: "Correlation of Radioactive and Chemical faecal fat determination in various Malabsorption Syndromes". *Amer. Jl. Med.* 30, 6, June 1961, pp. 927.
- Sheila Sherlock: "Liver and Pancreas — Medical". *Med. Annual*, 1958—59, pp. 69.
- Sun, D. C. H., Shay, H.: "Anevaluation of the Starch Tolerance Test in Pancreatic insufficiency". *Gastro-enterology*. 40, March 3, 1961, pp. 379.
- Twiss, J. R., Oppenheim, E.: *Liver, Pancreas and Biliary Tract*. 1955.
- Beeson, P. B.: "Leucine Aminopeptidase Activity". *Yearbook of Medicine*, 1959—60, pp. 579.

Doctor, my son has cholera, and worst of it is, he admits he caught it from kissing the maid ”.

Well, well young people do thoughtless things, don't they ? ”

“ Yes, but Doctor, I've been kissing the maid myself ”.

“ Too bad ”.

“ And what's more, I've been kissing my wife ”,  
What? Oh, my, gosh! Now we'll all have it ”.

\* \* \* \*

A young doctor just starting practice was invited to the home of a prominent hostess for dinner one night.

During coffee in the drawing room, the host asked him if he was enjoying himself.

“ Well, I should say so ”, beamed the physician.

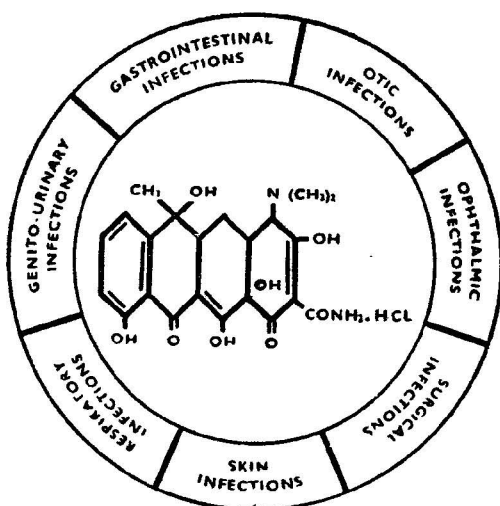
“ Not, only was the dinner delicious, but your wife sat me between two ladies whose children haven't had their tonsils removed yet. (J. A. M. A., The Bright Side).

— Courtesy - Unichem Medical Notes.

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# SOME ASPECTS OF ANXIETY STATE\*

A. VENKOBA RAO, M. D., D. P. M.,

Asst. Professor of Mental Diseases, Stanley Medical College & Asst. Surgeon,  
Government Mental Hospital, Madras.

It has been customary from the time of Kant to recognise three great divisions of mental phenomena which are typified by knowledge, desire and feeling, i. e. cognition, connotation and affect. Affect is also called emotion, mood or feeling tone. Some have been of the opinion that there is no value in this three fold division of mental contents. But in practice it is useful to retain this division. A psychiatric patient may manifest signs and symptoms pertaining to any or all the three of these mental faculties. The mind is capable of a variety of affective responses—happiness, sadness, suspicion, irritability, anger, and jealousy are some of them. Anxiety too is a common affective response. A normal mind reacts with any of these responses within 'physiological' limits. Thus to be anxious is not abnormal. Anxiety within physiological limits is useful to the experient. The latter's motivation for work is enhanced and consequently his achievement is of superior quality. Without a responsible degree of anxiety the person is prone to apathy and placidity. But anxiety assumes a pathological significance whenever it interferes with the mental and physical health of the individual.

Claude Bernard spoke of "internal environment" and developed a concept of "physiological homeostasis"—i. e. a state of equilibrium. Similarly the existence of "psychological homeostasis" has been hypothecated—i. e. a state of "mental equilibrium". In

the event of "disequilibrium", the primary response of the mind is anxiety. Thus anxiety is the basic response of a troubled mind. To restore "equilibrium" certain mechanisms operate and are termed "ego mechanisms" or "defence mechanisms". This subject of mental mechanisms we owe to Sigmund Freud. The present paper does not concern itself with this topic of "defence mechanisms", important though it is.

Anxiety state is a common psychiatric syndrome. Anxiety state, hysteria, obsessive compulsion states, hypochondriasis and reactive depressions are sub-headed under a group called "psychoneuroses". They are also called "minor psychiatric disorders" as opposed to "major psychiatric disorders" (the so called psychoses) such as schizophrenia, maniac depressive psychosis, etc. Apart from its academical implications, this terminology is not useful from a practical consideration. For example, a life long intractable anxiety, rendering the sufferer a permanent invalid, is called a 'minor' illness; whereas a short psychotic episode followed by a complete remission is nomenclatured as 'major'. The fallacy is thus clear.

It is uncommon to encounter cases of 'anxiety state' in pure culture in general practice. Nevertheless they do occur. More common are cases which masquerade as cases for

\* Based on an address delivered to the members of the Tiruchi Branch of the Indian Medical Association at Trichy on January 27th, 1962.



internists and specialists. It is the "somatization" of anxiety in them that render them mimic organic cases clinically. Frank anxiety is absent or nascent in these cases and it expresses itself through any organ-e.g. digestive, cardiovascular, respiratory, etc. It is here that one enters the field of "psychosomatic" medicine.

Anxiety is spoken of in at least two connotations. It may be a symptom in any illness-psychiatric or organic; or it may be a clinical entity per se "anxiety state". Anxiety is come across in various psychiatric illnesses, depressive psychosis, involutional psychosis, schizophrenia and others. An intractable anxiety state in an adolescent or adult may be a precursor of a schizophrenic illness. Among the various organic causes, anxiety occurs in arteriosclerosis, thyrotoxicosis, parkinsonism, spontaneous hypoglycemias, paroxysmal tachycardia, intracranial tumours, and administration of insulin and tranquillisers.

What causes psychogenic anxiety? Anxiety is generally the offspring of psychological conflicts. The word conflict is used to mean two opposing impulses. This 'conflict' is said to lie at an 'unconscious' level in the mind. In such cases, the treatment is aimed at 'floating' it upwards and making it reach the 'conscious threshold' of the patient. This process itself ameliorates or relieves completely the anxiety. But the source of anxiety need not always be a conflict, nor these conflictual points be situated in the patient's 'unconscious'. Several times the causes are obvious and lie within the patient's awareness. The conflicts may result from any degree of maladjustments of the individual. These maladjustments are

usually in the following spheres: Interpersonal; Work problems; Value problems; Cultural problems. Marital difficulties constitute the bulk of the interpersonal maladjustment forming the breeding ground for conflict eventually culminating in anxiety. Similarly conflicts over work, ethical and cultural problems. The patients may be only unaware of the causal connection between them and anxiety. In certain cases, the cause extends far back into the patient's past and takes its roots from a traumatic incident which has been lying in the depths of the patient's 'unconscious'. In such cases, therapy consists in unearthing the 'incident' and in this process, enabling the patient to 're-experience' the emotions that coloured the 'incident'. This technique called 'abreaction' works well in illnesses of recent duration. Freud and his followers attributed anxiety to the incomplete gratification of the sexual impulse. Another view has been the transmission of maternal anxiety to the child in the birth canal. Pavlovians believe anxiety to be a conditioned response and adopt 'deconditioning' technique in the treatment of anxiety syndrome. There are other explanations of anxiety from various schools and discussion of them is out of place here.

Anxiety is characterised by a subjective feeling of discomfort, gnawing tension, uneasiness, a constant expectation of the worst; the individual wonders whether anything has gone wrong with him or others. He wears a worried and a strained look; he is fidgety and restless; he is unable to relax and concentrate; he tends to forget and to commit mistakes; fatigue becomes his second nature; bodily aches and pains are felt; muscular twitchings are common. Palms and soles are wet with

cold sweat. Finger tremors are noticed. Fear of insanity is a dominant symptom in some cases.

At this point, let me discuss some of the common symptoms and manifestations of anxiety syndrome.

**Insomnia:** This is a common complaint in practice. The insomnia pattern of an anxious individual is characteristic. He goes to bed at the usual hour, but fails to fall asleep. Anxiety and worries prevent him from achieving sleep. At last he falls asleep late in the night. He then sleeps well, unless disturbed by frightening dreams and wakes up refreshed in the morning. This type of insomnia is to be differentiated from insomnia of a depressive patient whose difficulty lies not in falling asleep but regaining sleep after waking up late in night or in the small hours of the morning. He does not feel fresh when waking up. This differentiation helps to diagnose the condition accurately and also to choose an appropriate pharmacological agent to counter the difficulty. Some anxious individuals do not sleep to avoid experiencing bad dreams or even a nocturnal emission. To some sleep, implying inactivity, signifies death. So, sleeplessness is common among those who suffer a fear of death as a leading symptom. It is also common to come across patients who complain of sleeplessness even though they sleep well.

**Head Ache:** Anxiety state should never be forgotten as a cause of this another common complaint. This does not preclude a detailed investigation for a more serious organic cause such as intracranial tumours as has been already mentioned as causing symptomatic anxiety. Commonly anxiety head aches are treated for sinusitis, refractive errors, histamine

headache, etc. Such patients being unhappy and credulous form a ready market for the ever increasing pain killers. The 'ache' component of the symptom is usually not complained of. It is usually a discomfort, tension, 'ballooning' like, pricking sensation, heaviness or feeling of heat and cold in the head. In some, the sensation of something passing through the vertex is felt. Some of my patients have described the sensation as 'tic-tic' which denoted the vascular throb. The head ache may resemble that of migraine or trigeminal neuralgia. Head ache may occur in any other psychiatric syndromes. Trigeminal neuralgia in depressives has been well authenticated (Olivecrona).

"Mr. J. was being treated for pain in the back of the neck and occiput and vertex for nearly two years. Later a psychiatric examination revealed that the patient's complaint followed an assault over his head with a foot-wear by a business opponent. The patient was a successful contractor with a good standing. Loss of prestige, honour and security loomed large before him following the assault. Anxiety set in and the head ache was very prominent. This case reveals two other interesting features. As a container of brain and the seat of mind, great significance is imparted to the head. A small injury is likely to make one feel that damage has been wrought upon the brain. Secondly a foot wear, as an instrument to wreck vengeance has a great psychological implication. The psychological implications of the patient's head ache thus becomes obvious".

Such cases are common among those workmen who claim compensation for injuries. The above case illustrates

that the 'traumatic cause' need not lie in the 'unconscious' nor it be dated back several years.

**Cardiovascular Symptoms:** In some cases, somatization of anxiety occurs with the emergence of cardiovascular symptoms. Not infrequently such cases are mistaken for organic disorders. Precordial pain (more correctly infra-mammary pain), palpitation, tachycardia, 'hypertension', fear of heart disease, fear of sudden death are common manifestations. Investigation for organic causes for these has to be undertaken so as not to miss them. It is common to find a severe anxiety superimposed upon a cardiac disease - following myocardial infarction, diagnosis of hypertension, presence of a congenital heart, extrasystoles, auricular fibrillation. Pain over the precardium and in some cases in the shoulders and hand is common in anxiety states. Some of these patients are in the habit of counting their pulse, getting recorded their blood pressure repeatedly with different practitioners. Due to vascular instability, they experience syncopal attacks which aggravate their anxiety about developing 'high blood pressure'.

A following case of mine reveals several interesting features:—

Mr. R. a successful building contractor suffered from pain in the precardium, left shoulder and left hand for 10 years. Pain at times alternated with a numbness over these areas. The numbness spread occasionally to the left lower limbs also. He was diagnosed and treated variously as 'latent thyrotoxicosis', 'myxoedema', 'hypertension', 'nerves', 'cardiac neurosis' and 'malingering'. A detailed history and examination revealed that he was normal until ten years ago when

his father developed an attack of coronary thrombosis. The patient 'R' used to see the visiting specialist enquiring his patient about the precordial pain, its reference to the shoulders, hand and record the blood pressure and pulse often. He developed a thromboembolic phenomenon and consequently a left sided hemiplegia. At this time, the patient 'R' was involved in a motorbike accident which caused a dislocation of his left shoulder. This reduced, the patient began to experience pain in his shoulder. He also began to count his pulse. His father expired after a second attack of coronary thrombosis. The patient 'R' was also informed that the 'blood pressure' was hereditary. From that time gradually he began to experience palpitation, heaviness in the chest, pain in the left shoulder, left hand and numbness in the left lower limb. Some doctors have informed him that he was suffering from blood pressure. Others have recorded a 'normal' pressure. The patient was harbouring a constant fear of sudden death. This case indicates a common course of a 'cardiac neurosis', the injury to the shoulder triggering the entire course. A genuine anxiety at the event of his father's illness turned morbid gradually with somatization in the cardiovascular system. It is to be remembered that an anxious mind is always an enquiring and an easily suggestible mind. Informed of the hereditary nature and observing the course of the illness in his father, the patient had suggested to himself that a cardiac patient suffers from the symptoms which got grafted upon him.

It is not uncommon to see cases in which anxiety has been iatrogenic caused by a hasty diagnosis and prescriptions by well-meaning physicians,

reading by patients of pseudo-scientific publications on heart diseases, etc. Mention must be made at this point, without unduly digressing, the prevailing opinion regarding the relationship between emotion and hypertension. Emotionally charged situations, by virtue of their capacity to activate vascular mechanisms underlying arteriolar constriction, may contribute to the onset of the disease, to the occurrence of the symptoms arising from the organic lesions of the disease and even to the acceleration of the hypertensive disorder. Some observers tend to implicate psychological problems as contributors along with other factors in the genesis of the basic 'hypertensive mechanism'. Such a role has not yet been demonstrated. The data to date indicates that psychological stress may and does drive or activate what might be termed 'hypertensive mechanism' regardless of the nature of the still unknown factor that may in the first place be responsible for the existence of such mechanisms in predisposed individuals. Mere psychotherapy has no curative value in hypertensives.

**Respiratory Symptoms:** I know of cases where anxiety has expressed itself to cause 'breathing anomalies' — dyspnoeic symptoms. Some workers consider emotional disturbances as causing the commonest form of dyspnoea. In some cases the diaphragm position is low and this necessitates an increased respiratory activity. Sighing, hyperventilation syndrome with an accompanying tetany, anxiety attack precipitating asthmatic attacks in a susceptible person are well known. I know a case of pulmonary tuberculosis who became anxious and hypochondriacal after the successful treatment of his pulmonary condition. His main

complaint was that he was short of breath due to a deficient air entry into the upper part of the left lung. In addition to this, his anxiety was worsened when he was advised that being tuberculous he should not indulge in any sexual activity; besides, he developed a phobia for travelling in a vehicle when he was criticised that others would be infected if he travels in a crowded bus. These successively had a cumulative effect in increasing his anxiety. Prolonged psychotherapy has ameliorated his symptoms.

**Gastro Intestinal Symptoms:** 'Brassy tongue' is a not an infrequent complaint. Dryness of the tongue and throat often occur and may impair deglutition. In some cases where a 'conversion' phenomenon has occurred, 'globus hystericus' may be complained of—a sensation as if a 'ball' is situated in the throat and blocking the contents while swallowing. Anorexia, belching, flatulence, constipation and diarrhoea are common cases. 'Dropped stomach', 'viscerop-tosis', 'lack of acid', 'spastic colon', 'colitis', 'diverticulitis', 'dyspepsias of various types' are the common labels of these patients in practice.

**Sexual Deficiency:** It is not possible to go into various other manifestations of anxiety. I shall briefly discuss sexual disturbances which are common in practice. Impotence is a fairly common symptom heard by a general practitioner. Anxiety is the commonest psychiatric cause and also commoner of all causes of impotence. Frigidity in women is said to be commoner than impotence in men. But in practice impotence cases outnumber. Fear of impotence rather than impotence is also common. In some cases, the general symptoms of

anxiety syndrome are associated with impotence, while in others the only complaint is sexual deficiency. This deficiency (broadly termed impotence) may involve any of the spheres-libido, erection, ejaculation or orgasm. Thus they are classified as libidinous, erective, ejaculatory or orgasmic types of impotence. Anxiety may cause any type of deficiency.

The emotional basis of this symptom was found in some of the following commoner factors among several others that I have come across:

Spermaturia, fancied abnormalities of the size and shape of the external genitalia, nocturnal emission, masturbation, coitus interruptus, and various other methods of family planning, premarital and extramarital sexual intercourses, premaritally and extramaritally acquiring V. D., fear of V. D., an intercourse with an elderly partner (discrepancy of age), intercourse during menstruation, hydrocele, varicocele, phimosis, surgical operation on or around the genitalia, e.g. hydrocele, hernia, vasectomy, hysterectomy, selective impotence, (i. e. impotence extramaritally while retaining potency with the married partner or vice versa), as has been classically exemplified in the case of Goethe, too is come across in some cases.

In every case of sexual deficiency, apart from examining and investigating for organic causes, a detailed psychiatric examination is imperative. One other factor to be borne in mind is the question of administration of some well known tranquilisers to these cases of anxiety with sexual deficiency. Drugs like chlorpromazine, reserpine, thioridazine cause impotence as a side effect. This along with another side effect namely severe

anxiety and restlessness (akatzia) may make the patient worse. Hence it is better to be cautious not to precipitate this "iatrogenic anxiety and impotence". Other aspects of this important subject of impotence will be discussed elsewhere (under publication by the author).

**Management:** Psycho therapy is the sheet anchor in the treatment of anxiety state. It may be of a simple supportive, educative, explanatory and re-assuring type. In chronic cases, it has to be a prolonged one. Rapport between the patient and the doctor is quite essential if psychotherapy is to succeed. It is to be remembered again that an anxious mind is an enquiring mind and also an easily suggestible mind. Hence in explaining, one should guard against suggesting wrong things and thereby producing iatrogenic anxiety. Deep analytical therapy is not usually indicated in an average case. Abreactive technics consist in making the patient re-live emotionally the past traumatic incidents. This is achieved either by intravenous thiopentone or methedrine or carbon-dioxide inhalation. These things relieve the patient considerably. De-conditioning is a useful technic in cases of phobias—for instance, fear of travelling in a bus. The patient may be taught certain relaxation exercises to ease the muscular tension. Environmental manipulations and corrections whenever indicated have to be undertaken.

Dr. Beumont has rightly said that a person who asks for a tonic requires a sedative. Barbiturates come in handy. Amylobarbitone —  $1\frac{1}{2}$  to 3 grains control an impending anxiety attack and relieve even the established attack. The mere possession of the tablet in the pocket acts as a good

prophylactic agent. While using barbiturate, the risk of the patient becoming an addict and its abuse for suicidal act should be determined. It has been wrongly held that anxiety cases do not manifest suicidal tendency. But in some cases a secondary depression may set in and pre-dispose to suicide. Insulin in small doses has been known to control anxiety state by its sedating influence. It is especially very useful in physically impoverished individuals. Ataractic drugs or tranquillisers used in small doses are useful. They are most useful in senile anxiety. However, these drugs produce anxiety, restlessness which may be mistaken as an indication for increasing the dose of the drug. The anxious patient is likely to become worse with this

state of affairs (mentioned already). In cases where depression is an associated feature, anti-depressives like Niamid, Nephentine sulphate, combination of dexedrine and Amytal and Imiprimine are useful. Administration of the E. C. T. is not very useful except in cases of associated depression and severe restlessness. In certain selected cases, where anxiety state becomes intractable with all the possible conservative methods, prefrontal leukotomy of a limited type, such as resection of the frontal pole can be undertaken with useful results. In cases where somatization of anxiety has occurred, these have to be treated on general lines suggested above in addition to special appropriate types of treatment.

*Macbeth* : Cans't thou not minister to the diseased mind  
Pluk from the heart the rooted sorrows  
Rage out the written troubles of the mind  
And with that sweet oblivious antidote?

*Physician* : Therein the patient has to treat himself.

*Macbeth* : Oh! Throw the psyche to the dogs!

The practitioner who is born with clinical sense is in the same category as the good farmer who, using eyes, ears, nose and touch, can size up the state of his beasts. The Developing of clinical sense or, perhaps, sensitivity, is possible enough, just as Wordsworth trained himself to become a poet, but the danger of losing even any inherent quality in this direction has steadily increased with the growth of X-ray and laboratory techniques. Hospital residence magnifies this danger, unless the young intern hears some fundamental wisdom from his senior colleagues. But his senior colleagues themselves have often renounced their birth-right and depend too much on the tests of the tritater and the shadows of Roentgen. Even if, as a medical student, he were taught the fundamentals of clinical examination, the man going into general practice will almost certainly have to relearn them, and make his own working rules, by which to measure up his patient's state. This is a personal matter, but of much importance that it is being emphasized. To look at the tongue, sure reflector of the stomach, to feel the pulse and, while holding the hand, test both heart and personality, to look at the eyes and estimate the tissue's texture—these, surely, are the primary factors of our clinical examination, and are the basic guides in determining the seriousness or otherwise of case before us.—  
Dr. S. R. Wilson.

— (Courtesy — Unichem Medical Notes).

# ABSTRACTS AND EXCERPTS

## A COMPARISON OF VARIOUS FORMS OF TREATMENT OF ACUTE VIRAL HEPATITIS

This paper contains a careful and detailed account of the investigation to evaluate the efficacy of various forms of treatment of viral hepatitis, carried out in 10 German clinics during the years 1956 to 1959. In order to set up comparable groups, 404 patients were chosen according to certain criteria. These patients were placed in the treatment groups (1) a described basic therapy only, and in the remainder basic therapy plus (2) intravenous acetyl-methionine-choline and sodium acetyl methionine, (3) prednisone, (4) BAL, (5) Vitamin B-12 and (6) thioctic acid. The main conclusion was that these treatments did not differ from one another when judged by duration of illness or length of stay in hospital. Prednisone did cause an earlier fall in serum-bilirubin concentration but did not reduce the length of stay in hospital, nevertheless it is recommended on clinical grounds to be used in severe cases and those in which improvement is delayed. The problem of treatment of viral hepatitis is not resolved and action must lie in prevention by hygienic measures and injection of gamma globulin.

— Kuhn, H. A. & Baur, H. *Deut. Med. Woch.* 85, 1956-65 (1960).

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## SERUM TRANSAMINASE ACTIVITY IN ACUTE INFECTIVE HEPATITIS—A COMPARISON OF THE PYRUVIC AND OXALACETIC TRANSAMINASES :

The authors estimated the levels of serum glutamic oxalacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) in 50 healthy patients and compared the levels with those found in patients with acute infective hepatitis. The levels in healthy patients ranged from 5 to 40 units per ml. SGOT and from 4 to 30 units for SGPT. In acute infective hepatitis, the levels were from 380 to 670 SGOT and 410 to 700 units per ml. SGPT in the first week, falling to normal in 5 to 8 weeks: similar levels were found in 2 patients thought to be suffering from anicteric hepatitis. The levels tended to be highest of all in clinically fulminant cases so that estimations of the two enzymes may be of value in prognosis.

— Mathur, Chakravarty and Agarwal. *J. Ass. Physicians India* 8, 520-526 (1960).

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## INFECTIOUS HEPATITIS :

*Studies of the Effect of Gamma Globulin and on the Incidence of Inapparent Infection.*

Four controlled studies in prophylaxis of infectious hepatitis with gamma globulin were made in an institution for mentally defective children in New York, in which the disease had been endemic for the last 7 years. In the first trial a single dose of 0.01 ml. gamma globulin per pound of body weight was followed by a  $2\frac{1}{2}$  fold reduction in incidence of hepatitis with jaundice in the patients under test compared with the controls. The same dosage given to adults (attendants) was found to be ineffective. In the 2nd and 3rd trials, 0.06 ml. per lb. was followed by a 10-fold and 30-fold reduction of overt jaundice. It was thus clear that the optimum prophylactic dose of gamma globulin is 0.06 ml. per lb. especially for older children and adults.



In a fourth trial a small group of newly admitted patients was studied for evidence of subclinical infection, by the use of the thymol turbidity, cephalin flocculation, and serum transaminase (SGOT) tests of liver function after receiving this dose. The interesting finding in this experiment was that inapparent hepatitis was very frequently present in this community in spite of gamma globulin and would have been undiagnosed but for these tests. The actual ratio of anicteric hepatitis to overt jaundice was 12:1. It would seem that passive-active immunity was being induced among the inmates on a large scale under the conditions of endemic infection present. Second attacks of hepatitis were observed in 4% to 8% of patients who had a previous episode of the disease.

— *Krugman, Ward, Giles & Jacobs. J. Amer. Med. Ass. 174, 823-830 (1960).*

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### VIRAL HEPATITIS (SERUM HEPATITIS):

During the period 1953-59, the blood transfusion department of Medical College, Amritsar, issued 18,247 bottles of blood and 251 bottles of plasma for use in the wards of V. J. Hospital. Ten cases of serum hepatitis were encountered. No case of serum hepatitis was recorded in 251 plasma transfusions. Improved methods for the control of viral hepatitis must await the development of efficient techniques for eliminating or inactivating hepatitis virus B. Elimination of donors with a history of jaundice may help in reducing the incidence of the disease.

— *Talwar. Ind. J. Med. Sc. 14, 943-948 (1960).*

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### CONTROL OF INFECTIOUS HEPATITIS IN A BOARDING SCHOOL BY GAMMA GLOBULIN:

In a special school for the educationally subnormal with 57 resident pupils, 2 cases of infectious hepatitis occurred and were sent to hospital. Within the next 10 days all the remaining children as well as the resident staff were injected with 2.5 ml. gamma globulin (under 10 years) and 5 ml. (over 10 years). This dosage averaged 0.048 ml. per lb. body weight for the boys, and 0.052 ml./lb. for the girls. The hygiene of the school was reviewed and paper towels provided.

Only 9 secondary cases occurred, all within 16 days of the gamma globulin injection. In view of the long incubation period of infectious hepatitis, it could be assumed that these 9 children were already incubating the disease when they were injected. All the cases were clinically mild. The abrupt termination of the outbreak could reasonably be attributed to its control by administration of gamma globulin to all the contacts.

— *Smith, C. M. Lancet, 1961, Oct. 7, 818-19. From Bull. of Hygiene.*

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### HEPATITIS:

Infectious hepatitis is one of the few important virus diseases of man for which no susceptible experimental host has been found. It is a serious cause of morbidity, particularly in times of stress, in populations with a high standard of hygiene, in much the same way as poliomyelitis, and is worthy of more intensive efforts to isolate the virus for study and development of prophylactic measures.



Certain hepatitis viruses may circulate in blood stream for long periods of time without causing obvious illness and may easily be transferred to other persons who are susceptible and develop the diseases. For this reason it is essential that transfusions of blood should be given only when essential, and extreme care must be taken to sterilize adequately all instruments used for injections or collection of blood. Meanwhile, efforts must be intensified to find methods of detecting the healthy carriers and inactivating the viruses in blood and blood products without injuring the blood.

— *F. O. MacCallum, Brit. Med. Bulletin—9, 225, 1953.*

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### CONSIDER THE COCO-NUT :

A new intravenous fluid, pyrogen-free, sterile, non-sensitizing, very cheap and plentiful in many places where artificial solutions may not be available, is reported by Harry S. Goldsmith, Chief of Surgery at the Seoul Military Hospital, Korea (*Brit. J. Surg.*, 49, 421-422, 1962). Coco-nut water was used intravenously during the 39-45 war by the Japanese in Sumatra and the British in Ceylon and several people have reported well of it. The fruit of *Cocos nucifera* is best cut at seven months old when its water is most sugary around 5 gm. per 100 ml. of glucose and fructose. The ends of the nut are cut back an inch or so, once it has been cleared for cracks in the shell with possible bacterial contamination, and the exposed meat is painted with alcohol. Sterile trocars are inserted and 500 to 900 ml. of fluid can be filtered into a sterile bottle, best used quickly, before bacteria take the chance to grow in it. Its ionic composition is akin to that of intracellular fluid with high potassium, low sodium, chloride and phosphate. It is, therefore, especially fitted for patients with diarrhoea, and it might anyway be useful under adverse conditions in the tropics.

— *Journal of R. A. M. C. 108, 2 1962.*

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### SECOND INTERNATIONAL CONFERENCE OF HUMAN GENETICS. (ROME 1961) :

J.B.S. Haldane and S. D. Jayakar in their paper on "An enumeration of some human relationships" dealt with the problem of human inbreeding, particularly with respect to first cousin marriages. They stated among other things that where two monozygotic brothers married two monozygotic sisters, and a pair of their children intermarried, the progeny should be as severely affected as those of a union between a full brother and a sister. The authors expressed the hope that the enumeration they presented was complete and that the symbolism they use would provoke discussion and hence improvement. They felt that the work on distant relationships, though not important in Europe and European communities were perhaps needed in South India, where the incidence of first cousin marriages among millions was 25%.

— *Ind. Journal of Pediatrics, 29, 14 1962.*

**COMPARATIVE TRIAL OF DRUGS IN BACILLARY DYSENTERY:**

Four treatment groups were listed in a random order keeping 20 patients to each group:

- Group 1: Sulphadimidine 2-G. initially followed by 1-G. six hourly for 5 days.
- Group 2: Sulphamethoxypyridazine (Lederkyn) 1-G. on the 1st day and 0.5-G. daily for 4 more days.
- Group 3: "Streptotriad", 3 tablets 3 times daily for 5 days.
- Group 4: Tetracycline ("Achromycin") 250 mg. six hourly for 5 days.

A comparative trial on the above regimens was carried out in bacillary dysentery caused predominantly by *Shig. flexneri*. The good comparability of treatment groups bacteriologically to sulphadimidine, sulphamethoxypyridazine and "Streptotriad" and that there was no difference in efficacy between the three latter drugs. It is concluded that tetracycline is the drug of choice, that sulphonamide-streptomycin combinations are unnecessary and that a long-acting sulphonamide may be used initially on grounds of cost followed by tetracycline if there is treatment failure.

—Bibile, S. W., Cooray, M. P. M., Balasubramaniam, K. and Gulasekaram, J. J. of *Tropical Medicine & Hygiene* 64, 300-302 (1961).

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**ENTERIC FEVERS:**

In this article clinical experience with 232 cases of enteric fever treated in hospitals in Nagpur and Jabalpur is described. Age varied from 3 years to 58 years; 210 were cases of typhoid fever, 18 of paratyphoid A and 4 of paratyphoid B. Chloramphenicol was well tolerated and gave good results without serious complications. Dosage of usually 50 mgm. per kgm. daily and this was applied in 3 schemes; in schemes 1 and 2 the drug was given for 3 and 7 days respectively after the temperature touched normal, and in scheme 3 it was given for 7 days along with TAB vaccine 0.1, 0.2 and 0.3 c.c. at 2-day intervals followed by 2 further doses (0.5 and 0.5 c.c.) after the drug was stopped. The relapse rate under scheme 1 and 2 was 35.2% and 14.8% respectively, while under scheme 3 it was only 2.2%. It is considered that such a combination of chloramphenicol and TAB vaccine gives the most satisfactory results, especially when the drug is started early in the disease.

—Mishra M. P. & Dave, D. S., *J. Ass. Physicians India* 9, 243-252 (1961).

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**ERADICATION OF INFECTIOUS DISEASES:**

There are many definitions of the term "eradication", which the author uses to mean extinction of the pathogen. On this definition no infection has yet been accomplished, which implies an unstable situation. Where preventive measures must be continued, only control has been achieved.

Basic requirements for eradication are discussed; they include political stability, popular support, adequate funds, personnel and equipment, and local staff for certain phases. A number of possible factors affecting eradication are discussed. For example the evolution of a human from an animal (bovine tuberculosis) can be eradicated, but not if the host is wild (yellow fever). Competition between related pathogens may permit only one to flourish; if this is eradicated, a competitor may appear. Established indigenous parasites and vectors are more difficult than those recently introduced. Reduction of the population of a deployed organism to a very low figure usually results in its eventual extinction because of in-breeding, but not in the case of haploid organisms. Spontaneous extinction may result from loss of fitness to survive.

Results of eradication campaigns are spectacular at first but final elimination is prolonged and difficult. Small islands are most suitable for such campaigns. Among diseases suitable for world eradication is smallpox.

Unexpected difficulties have arisen in malaria eradication and, even if this is accomplished, simian malaria may spread to man. In the case of poliomyelitis the replacement of wild strains by attenuated strains is suggested, but there are difficulties here also. Cholera can be eradicated by provision of pure water but paracholera may persist.

The author concludes that present obstacles to eradication may be resolved by techniques already under study and we may expect to be freed from the major infectious diseases within, say, 100 years.

— Cockburn, T. A. *Science* (1961), 133, 1050-1058.

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### CHECK LIST FOR DIABETES TREATMENT :

Because of its prevalence and chronicity, diabetes mellitus should be the continuing concern of all physicians, regardless of their type of practice. An essential part of treating the condition is teaching the patient how to live with it. As in any educational program, a systematic approach should be used. Each physician should have certain specific objectives clearly in mind as he teaches his diabetic patients.

To aid him, the American Diabetes Association has prepared the following check list of 9 basic elements of treatment, which constitutes a minimum program for diabetes management. There are many other aspects of treatment which are not mentioned; but they are not as important as the following :

1. Diet
2. Urine testing
3. Action of insulin and other hypoglycaemic agents
4. Technique of insulin injection and sites for it
5. Care of syringe and of insulin
6. Symptoms of hypoglycemia
7. Symptoms of uncontrolled diabetes
8. Care of the feet
9. What to do in case of acute complications.

This guide is not only of value in the initial education of a new diabetic, but can also be most helpful to both patient and physician in the subsequent years of management.

— American Diabetes Association, *J. A. M. A.* Nov. 25, 1961.

**PYREXIA OF UNKNOWN ORIGIN:**

All patients with fever of obscure cause need to be thoroughly interrogated on its mode of onset as well as on the leading symptoms, such as cough or pain. They should be examined with particular attention to the skin, joints, lymph nodes, heart, throat, abdomen, and pelvis. Then a chest-radiograph, blood count, measurement of erythrocyte sedimentation rate, and microscopical examination of urinary deposits must be done. When considering further investigations it is well to bear in mind the old principle—think first of uncommon manifestations of common diseases rather than of rare diseases. Tuberculosis of the peritoneum, liver, or lymph nodes, or even miliary tuberculosis must always be suspected. Examination of the retinae for tubercles, liver biopsy, and laparotomy in that order may provide the necessary evidence, but occasionally the therapeutic response to isoniazid is the only way of clinching a clinical probability. A therapeutic trial of this description is justified only if the treatment will not obscure the clinical picture should the diagnosis be other than that under test. For example short courses of antibiotics given haphazardly may delay the diagnosis of bacterial endocarditis by making the blood cultures negative.

Endocarditis is a notorious deceiver, and patients with it have died without a cardiac murmur, a detected embolus, or a positive blood culture to their epitaph. Another trap for the unwary is the solitary liver abscess, or the paracolic, pelvic, or renal abscess without local symptoms or signs. Such conditions are met with most frequently in elderly diabetic patients or debilitated patients with diverticulitis or chronic disease of bladder or biliary apparatus, and in them a laparotomy should not be shirked. Low grade pyaemia without endocarditis is occasionally encountered in patients with cirrhosis of liver and with the rheumatoid syndrome. In all these conditions neutrophilic leucocytosis or a shift to the left with many stab cells may point to the possibility of sepsis. A blood count is also helpful in glandular fever, which sometimes occurs without sore throat, rash, or enlarged nodes, and in which neutropenia or atypical "glandular-fever cells" may be noted. It may also help in brucellosis, where neutropenia is common. Virus infections, with the exception of psittacosis (a very toxic illness with pulmonary complications), do not cause fever of more than three weeks' durations.

Among the neoplastic diseases the leukaemias and the reticuloses are the best known causes of fever, but we must also remember hypernephroma and carcinoma of stomach, liver, and pancreas, especially in young people. Leukaemoid or eosinophilic blood pictures may be found in carcinomatous patients.

The hypersensitivity and collagen diseases are the modern diagnostician's nightmare for even a case of erythema nodosum due to sarcoidosis may not declare itself for weeks, and not every patient with disseminated lupus erythematosus has L. E. cells in the blood, nor has every patient with polyarteritis nodosa hypertension, albuminuria, and eosinophilia. Elderly patients with giant cell arteritis, who might be expected to have headache and tender nodules on the scalp, may in fact suffer only from fever, anorexia, muscle pains, and wasting. Febrile rheumatoid disease may linger in the muscles for months before declaring itself in the joints. It is as well to remember, too, that thrombophlebitis, pulmonary infarction, and myocardial infarction may all cause persistent low-grade fever.

Early diagnosis in cases of obscure fever is of great importance, whether to allay apprehension or to enable correct treatment to begin. Yet it can be one of the most difficult exercises of skill and imagination for the physician.

## **RULES GOVERNING THE MADRAS CLINICAL JOURNAL**

In exercise of the powers vested in it under Rule 26 of the Rules of the Madras State Branch of I. M. A. and with the approval of the Central I. M. A. in accordance with Rules 8, Part II, Rules of the I. M. A. (Central), the Council of the Madras State Branch of the Indian Medical Association, has framed the following rules for the governance and proper conduct of its journal - the Madras Clinical Journal :—

1. The Madras State Branch of the Indian Medical Association, by itself or through any of its constituent branches, may publish and circulate a journal, which shall be the official organ of the Madras State Branch of I. M. A., of a character specially adapted to the needs of the medical profession in the State and which shall undertake publicity and propaganda work of the Association through its columns and publish other literature in accordance with the objects of the Association. The Journal shall be called "THE MADRAS CLINICAL JOURNAL" and shall be supplied to all the members of the Madras State Branch free of cost.

2. In the event of any of its constituent branches coming forward to run the journal as per rule 1, the State Council have the discretion to permit the said constituent branch to manage and run the journal on its own responsibility for such period as may be determined by the State Council at its annual meeting; and in such case the local branch taking up the responsibility of running the journal shall do so subject to the following provisions of sub-rules :

The Editor of the journal shall —

(a) respect the dictum of the central office of I. M. A. and refrain from writing any editorial in the journal.

(b) reserve two pages in each issue of the journal and one page in any of its four cover pages for propaganda, publicity, organisational matters and other special news or announcements of the Madras State Branch of I. M. A. in general, to be at the disposal of the hony. secretary of the Madras State Branch. In the absence of such matter, this space can be utilised by the Editor for other purposes.

(c) prepare a budget estimate and submit it through the branch Secretary to the hony. secretary of the State Branch for consideration and sanction at the annual meeting of the State Council.

(d) prepare a quarterly statement of accounts of the journal and submit the same to be placed before the quarterly meetings of the State Council through the branch secretary to the hony. secretary of the State Branch.

(e) prepare an yearly statement of accounts and get it audited by an auditor appointed by the managing committee of the journal and submit it through the branch secretary to the hony. secretary of the State Branch before the annual meeting of the State Council. Such audited statements of accounts for each year shall be published in the journal as soon as possible after the audit.

(f) have power to spend money for various purposes connected with the journal upto the amount sanctioned in the budget estimate for the year by the State Council. Expenditure in excess of this limit shall require the ratification by the State Council.

(g) make available copies of the journal to the members of the medical profession in and outside the Madras State who are not members of the Madras State Branch of I. M. A. on an annual subscription of Rupees (6-00) Six only, the subscription rate being liable to be varied by the State Council from time to time.

(h) The Madras State Branch of I. M. A. shall be entitled to a contribution of 25% on the surplus income over expenditure in each year when such surplus is over Rs. 500/- and below Rs. 2000/- and of 33 1/3rd% when the surplus is over 2000/-. The surplus shall be determined with reference to the surplus as declared in the annual audited statement of accounts of the journal.

(i) In the event of any loss incurred by the local branch in running the journal, the Madras State Branch of I. M. A. also shall bear the loss in the same proportion as the surplus is shared between the local branch running the journal and the Madras State Branch of I. M. A.

(j) The local branch running the journal shall constitute a managing committee of nine members consisting of 7 members from the local branch and two members elected by the State Council from among the members of the other local branches in the State. The two members of the State Council shall be paid T. A. for attending the meetings of the committee from the funds of the journal.

3. In the event of no local branch coming forward to run the journal under this rule, the management and administration of the journal shall be carried on by the Madras State Branch of I. M. A. as provided for under the following sub-rules; and the hony. secretary of the State Branch shall take all necessary steps in this regard:

(a) The journal shall be under the general supervision and control of the State Council of the Madras State Branch of I. M. A. represented by the hony. secretary of the State Branch.

(b) The administration of the Journal shall be under the charge of a journal committee.

(c) The Journal Committee shall consist of the following —

(i) The President of the Madras State Branch of I. M. A.

(ii) The Editor (who shall also be the Convener)

(iii) Two Assistant Editors

(iv) Four members elected by the State Council

(v) The Hony. Secretary of the State Branch

(d) The Editor, two assistant Editors and the four members of the journal committee shall be elected at the annual meeting of the State Council; and on such election, the Editor and two assistant Editors shall hold office for a period of 3 years, and the elected four members for a period of one year. The State Council shall have power to fill up the vacancies of office by death, resignation, etc., by nomination according to a decision of the majority and such nominees shall hold their office for the remaining period of the tenure of office which shall be clearly specified.

(e) The journal committee shall —

- (i) help the Editor in the regular publication of the journal.
- (ii) meet once in three months at the time of the meeting of the State Council.
- (iii) scrutinize all the articles to be published in the journal and edit, pass or refuse them for publication.
- (iv) be responsible for the management of the business of the journal, its printing, securing of advertisements, distribution of the journal among the members, etc.
- (v) have power to elect referees and collaborators.
- (vi) reserve two pages in each issue of the journal and one page in any of its four cover pages for propaganda, publicity, organisational matters and other special news or announcements of the Madras State Branch of I. M. A. in general, to be at the disposal of the hony. secretary of the Madras State Branch. In the absence of such matter, this space can be utilised by the journal committee for other purposes.
- (vii) prepare a budget estimate and submit it through the hony. secretary of the State Branch for consideration and sanction at the annual meeting of the State Council.
- (viii) prepare a quarterly statement of accounts of the journal and submit the same to be placed before the quarterly meetings of the State Council through the hony. secretary of the State Branch.
- (ix) prepare an yearly statement of accounts and get it audited by an auditor appointed by the State Council and submit it through the hony. secretary of the State Branch before the annual meeting of the State Council. Such audited statements for each year shall be published in the journal as soon as possible after the audit.
- (x) have power to spend money for various purposes connected with the journal upto the amount sanctioned in the budget estimate for the year by the State Council. Expenditure in excess of this limit shall require the special prior sanction of the State Council.
- (xi) make available copies of the journal to the members of the medical profession in and outside the Madras State who are not members of the Madras State Branch of I. M. A. on an annual subscription of Rupees (6-00) Six only, the subscription rate being liable to be varied by the State Council from time to time

(f) The Madras State Branch of I. M. A. shall have a responsibility in the profit and loss in running the journal. In the event of any profits as determined in the annual audited statement of accounts for each year, the Madras State Branch of I. M. A. shall apportion 25% of the nett profits to the general funds of the State Branch and the rest of the amount as reserve fund in the name of the journal.

(g) The Editor of the journal shall —

- (i) be the chairman of the journal committee in the absence of the president.
- (ii) be responsible with the help of the journal committee for the publication and management of the journal.
- (iii) have the discretion of condensing, correcting any of the articles passed for publication by the journal committee.
- (iv) help the journal committee for the preparation and submission of the budget and other statements of accounts as per sub-rule (e) (vii) (viii) and (ix) to the State Council through the hony. secretary of the State Branch, in time.

4. Save in so far as is expressly provided for herein, the management of the affairs of the Madras Clinical Journal, the official organ of the Madras State Branch of I. M. A. shall vest with the State Council of the Madras State Branch of I. M. A which shall have power to amend, alter or vary these rules or frame any other rules as may, from time to time, seem necessary or expedient to the State Council in the best interests of its journal.

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